

REMARKS

The foregoing Preliminary Amendment is requested in order to delete the multiple dependent claims and avoid paying the multiple dependent claims fee.

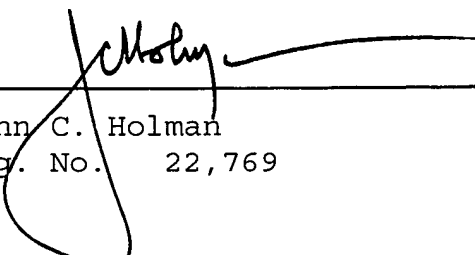
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned " VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Early action on the merits is respectfully requested.

Respectfully submitted,

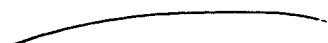
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (amended) A chemical compound or composition according to claim 1 [or claim 2] wherein successive N $\alpha$ -substituted  $\alpha$ -L-amino-acid residues in the  $\beta$ -strand-forming section of peptide are separated from each other by single N $\alpha$ -unsubstituted  $\alpha$ -L-amino-acid residues, such that the  $\beta$ -strand-forming section of peptide comprises an alternating sequence of N $\alpha$ -substituted and N $\alpha$ -unsubstituted  $\alpha$ -L-amino-acid residues.

4. (amended) A chemical compound or composition according to claim 1 [any preceding claim] wherein the N $\alpha$ -substituent of each N $\alpha$ -substituted  $\alpha$ -L-amino-acid residue in the  $\beta$ -strand-forming section of peptide sterically allows or promotes the  $\beta$ -strand-forming section of peptide to form a  $\beta$ -strand, and sterically hinders the association of the said second edge of that  $\beta$ -strand with another  $\beta$ -strand.

6. (amended) A chemical compound or composition according to claim 4 [or claim 5], wherein the N $\alpha$ -substituent of each N $\alpha$ -substituted  $\alpha$ -L-amino-acid residue in the  $\beta$ -strand-forming section of peptide is selected from the group consisting of:

- a fluorine atom or an OH group;
- a group that is connected to the N $\alpha$  atom by an oxygen atom within it;
- a group that is connected to the N $\alpha$  atom by a CH<sub>2</sub> subgroup within it;
- a methyl or ethyl group, or some other alkyl or aliphatic group;
- a substituted or unsubstituted benzyl group, or some other arylmethyl group;
- an acetylated or acylated 2-hydroxy-4-methoxybenzyl (AcHmb) group; and

an acylated or unacylated 2-hydroxybenzyl (AcHb/Hb) group.

7. (amended) A chemical compound or composition according to claim 1 [any preceding claim], wherein the side chain of each  $\alpha$ -L-amino-acid residue in the  $\beta$ -strand-forming section of peptide allows or promotes the  $\beta$ -strand forming section of peptide to form a  $\beta$ -strand.

10. (amended) A chemical compound or composition according to claim 7 [any one of claims 7 to 9], wherein the side chain of one or more  $\alpha$ -L-amino-acid residues in the  $\beta$ -strand forming section of peptide is selected from the group consisting of:

- a hydrophobic group, or a group that has a considerable hydrophobic portion;
- a branched or unbranched alkyl or aliphatic group;
- a group that is branched at its connecting  $\beta$ -carbon atom;
- an aromatic group;
- an acidic or basic group; and
- an amide- or hydroxyl-containing group.

11. (amended) A chemical compound or composition according to claim 1 [any preceding claim], wherein the side chain of one or more  $\alpha$ -L-amino-acid residues in the  $\beta$ -strand-forming section of peptide hinders the stacking of  $\beta$ -sheets.

13. (amended) A chemical compound or composition according to claim 1 [any preceding claim], wherein the side chain of one or more  $\alpha$ -L-amino-acid residues in the  $\beta$ -strand-forming section of peptide allows the compound or composition to be traced or detected.

15. (amended) A chemical compound or composition according to claim 1 [any preceding claim], wherein the side chain of one or more  $\alpha$ -L-amino-acid residues in the  $\beta$ -strand-forming section of peptide is selected from the group consisting of the side chain of:

any naturally occurring  $\alpha$ -L-amino-acid or synthetic derivative thereof; glycine; alanine; serine; cysteine; threonine; valine; leucine; isoleucine; methionine; phenylalanine; tyrosine; tryptophan; glutamine; asparagine; glutamate; aspartate; histidine; lysine; arginine; and tert-leucine or  $\beta$ -hydroxyvaline.

16. (amended) A chemical compound or composition according to claim 1 [any preceding claim] wherein the target  $\beta$ -strand is formed by the Alzheimer's A $\beta$  peptide, and the  $\beta$ -strand-forming section of peptide binds specifically as a  $\beta$ -strand to part or all of the KLVFFAE sequence within the target  $\beta$ -strand in the parallel orientation, thereby forming a parallel  $\beta$ -sheet complex wherein consecutive residues of the  $\beta$ -strand-forming section of peptide lie directly opposite consecutive residues of the KLVFFAE sequence in the same order.

17. (amended) A chemical compound or composition according to claim 1 [any one of claims 1 to 15] wherein the target  $\beta$ -strand is formed by the Alzheimer's A $\beta$  peptide, and the  $\beta$ -strand-forming section of peptide binds specifically as a  $\beta$ -strand to part or all of the KLVFFAE sequence within the target  $\beta$ -strand in the antiparallel orientation, thereby forming an antiparallel  $\beta$ -sheet complex wherein consecutive residues of the  $\beta$ -strand-forming section of peptide lie directly opposite consecutive residues of the KLVFFAE sequence in reverse order.

19. (amended) A chemical compound or composition according to claim 1 [any preceding claim] wherein the  $\beta$ -strand-forming section of peptide is preceded by, followed by, or otherwise attached to a distinct membrane-penetrating section of peptide which enables the  $\beta$ -strand-forming section of peptide to cross biological barriers such as cell membranes and the blood-brain barrier.

21. (amended) A chemical compound or composition as claimed in claim 19 [or claim 20] wherein the membrane-penetrating section of peptide is made resistant to enzyme-catalysed proteolysis by the inclusion of  $\alpha$ -D-amino-acid residues and/or N $\alpha$ -substituted amino-acid residues.

22. (amended) A chemical compound or composition according to claim 1 [any preceding claim] wherein the  $\beta$ -strand-forming section of peptide has a free or acylated N terminus and a free, amidated, or esterified C terminus, or forms part of a larger peptide which has a free or acylated N terminus and a free, amidated, or esterified C terminus.

23. (amended) A chemical compound or composition according to claim 1 [any preceding claim] wherein the  $\beta$ -strand-forming section of peptide is attached to another functional component.

25. (amended) chemical compound or composition according to claim 23 [or claim 24], wherein attachment of the  $\beta$ -strand-forming section of peptide to the functional component is by means of an amide or ester linkage formed with the C-terminal carboxyl group or N-terminal amino group of the full peptide, or with a carboxyl, amino, or hydroxyl group of a side chain within the full peptide, or by means of a disulphide bridge formed with a thiol group of a side chain within the full peptide.

26. (amended) A chemical compound or composition according to claim 1 [any preceding claim] wherein the  $\beta$ -strand-forming section of peptide associates with a target  $\beta$ -strand comprising the amino-acid sequence KLVFF (SEQ. ID. NO. 1).

27. (amended) A chemical compound or composition according to claim 1 [any preceding claim] comprising one or more components which mimic the structure and action of said  $\beta$ -strand-forming section of peptide, wherein the components are formed by replacing one or more of the backbone peptide groups or side-

chain groups of the  $\beta$ -strand-forming section of peptide by another chemical group of similar stereochemistry and ability to form favourable non-covalent interactions with the target  $\beta$ -strand.

29. (amended) A method for inhibiting or reversing the association of a target  $\beta$ -strand into a  $\beta$ -sheet or  $\beta$ -fibre, comprising exposing the target  $\beta$ -strand to a chemical compound or composition according to claim 1 [any preceding claim] and allowing or inducing the chemical compound or composition to associate with the target  $\beta$ -strand.

30. (amended) The use of a chemical compound or composition according to claim 1 [any one of claims 1 to 28] in the manufacture of a medicament for inhibiting or reversing the association of a target  $\beta$ -strand into a  $\beta$ -sheet or  $\beta$ -fibre.

31. (amended) A method for inhibiting or reversing the aggregation of proteins or peptides, comprising contacting the proteins or peptides with a chemical compound or composition according to claim 1 [any one of claims 1 to 28].

32. (amended) The use of a chemical compound or composition according to claim 1 [any one of claims 1 to 28] in the manufacture of a medicament for inhibiting or reversing the aggregation of proteins or peptides.

33. (amended) A method for assisting in the refolding of denatured or aggregated proteins or peptides, comprising contacting the aggregated proteins or peptides with a chemical compound or composition according to claim 1 [any one of claims 1 to 28].

34. (amended) The use of a chemical compound or composition

according to claim 1 [any one of claims 1 to 28] in the manufacture of a medicament for assisting in the refolding of denatured or aggregated proteins or peptides.

35. (amended) The use of a chemical compound or composition according to claim 1 [any one of claims 1 to 28] in the preparation of a composition for the diagnosis, study, or treatment of a disease caused by the aggregation of proteins or peptides.

36. (amended) A method for inhibiting the oligomerisation or association of protein subunits, comprising exposing the protein subunits to a chemical compound or composition according to claim 1 [any one of claims 1 to 28].

37. (amended) The use of a chemical compound or composition according to claim 1 [any one of claims 1 to 28] in the manufacture of a medicament for inhibiting the oligomerisation or association of protein subunits.

38. (amended) The method of claim 36 [or the use of claim 37] applied to inhibit the oligomerisation of an enzyme whose catalytic activity depends on its oligomerisation by the association of  $\beta$ -strands.

39. (amended) A method for indicating the presence or location of  $\beta$ -strands,  $\beta$ -sheets, or  $\beta$ -fibres, comprising exposing a test sample to a chemical compound or composition according to claim 1 [any one of claims 1 to 28] which comprises a detectable moiety.

40. (amended) The use of a chemical compound or composition according to claim 1 [any one of claims 1 to 28] which comprises a detectable moiety, in the manufacture of an agent for indicating the presence or location of  $\beta$ -strands,  $\beta$ -sheets, or  $\beta$ -fibres.

41. (amended) A method for affinity or protein-renaturation chromatography, comprising the steps of covalently attaching a chemical compound or composition according to claim 1 [any one of claims 1 to 28] to a solid matrix, resin, or support; passing a test sample over the column; and separating the desired treated product from the column.

42. (amended) A combinatorial library comprising chemical compounds or compositions according to claim 1 [any one of claims 1 to 28].

43. (amended) A pharmaceutical compound or composition according to claim 1 [any one of claims 1 to 28].

44. (amended) A method of diagnosing, studying or treating a disease caused by the aggregation of proteins or peptides, comprising contacting the proteins or peptides with a chemical compound or composition according to claim 1 [any one of claims 1 to 28].